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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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09/375,248 08/16/99 FERRELL R 28967/35255A

MARSHALL O'TOOLE GERSTEIN
MURRAY & BORUN
6300 SEARS TOWER
233 SOUTH WACKER DRIVE
CHICAGO IL 60606-6402

HM22/1010

EXAMINER

SORBELLO, E

ART UNIT

PAPER NUMBER

1633

DATE MAILED:

10/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/375,248

Applicant(s)

FERRELL ET AL.

Examiner

Eleanor Sorbello

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 July 2001.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 14-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 19 is/are allowed.
- 6) ☒ Claim(s) 1-11, 14-18, 20 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received. .
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

Response to amendment

1. Applicant's amendment and response to the official Office Action mailed February 14, 2001 as Paper No. 12, has been received and filed on July 19, 2001 as Paper No. 14. Claim 1 has been amended, claims 12,13 and 22-36 have been canceled. **Claims 1-11, 14-21 are pending.** Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's argument.
2. Applicant's arguments are addressed below on a per section basis.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. Claims 1-11, 14, 15, 18, 20, 21 remain rejected as stated in Office Action dated 2/14/01 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue on pages 2-7 of Response dated July 19, 2001 that the written description of the alleles representative of those predictive of hereditary lymphedema should be removed because examiner has focussed on the fact that (a) the genus of

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VEGFR-3 alleles are not represented by SEQ. ID. No: 1 and (b) DNA/allele subject matter.

Examiner argues that the amended claims are directed to determining if a human subject is at risk for developing hereditary lymphedema by assaying the nucleic acid of the subject to determine the presence or absence of a mutation that results in a change in the amino acid sequence of one VEGFR-3 allele.

Applicants argue that they have described the invention adequately and that the specification provides "a" human VEGFR-3 coding sequence. (See page 3, last paragraph). They argue that the reference sequence can be used to compare any human subject's sequence, in looking for mutations that alter the coding sequence.

However, examiner argues that applicants have described only one VEGFR-3 allele and that applicants are not in possession of all VEGFR-3 alleles present in the population. Applicants have described the VEGFR-3 allele of the instant invention having mutations at 5 positions. Therefore, applicants are in possession of only the VEGFR-3 allele encoded by SEQ. ID. NO: 1 with mutations at nucleotide substitutions at specified positions, namely C3360T, G2588A, G3141C, T3150C and G3164A but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Applicants argue that they are not claiming a genus of VEGFR-3 alleles but that their invention is directed to a method for determining the presence or absence of a mutation in one or more of a human subject's VEGFR-3 alleles. (See page 5, lines 7). However, examiner argues that it is not clear if there is value in screening a population

for the presence or absence of mutations which are allegedly reflective of a disease condition when only one allele (out of a whole genus of alleles being present in a population) is known, and described. It is not clear if the other alleles will have other mutations which are not described in the instant invention which will be indicative of hereditary lymphedema.

Applicants argue that the examiner has made a rejection based on the recitation of the phrase "at least one allele", and that applicants were not claiming a genus of polynucleotides that comprise the VEGFR-3 alleles, but simply indicating that at least one of the two alleles present in the individual. Examiner however, argues that this language may be incorporated into the claim to more adequately describe what applicants intended.

Applicants argue that all they are claiming (i) a screening method and that fore-knowledge or description of the all VEGFR-3 alleles is not required even though many are taught in the specification, and (ii) how one is to draw conclusions based on the method used. (See Response page 6, paragraph 2). However, examiner agrees that the applicants are claiming a method for screening for familial lymphedema by detecting the mutations described in SEQ. ID. NO: 1, and not for any and all mutations not described in the application and present in other alleles.

Applicants argue that the product claims of 14, 15, 18, 20 and 21 are also rejected under the written description provision but that they are not directed at alleles, but are directed to oligonucleotides, kits, and arrays. (See Response page 6, last paragraph).

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Examiner argues that the claim recites that if any one nucleotide is different to the wild type it can be used as a probe. However, examiner argues that applicant claims any one nucleotide difference, which does not adequately describe the specific difference that is being claimed, therefore applicant is not in possession of that which is claimed.

Therefore, claims 1-11, 14, 15, 18, 20, 21 remain rejected.

5. Claims 1-11, 14, 15, 18, 20, 21 remain rejected as stated in Office Action dated 02/14/01 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a method of screening for an increased risk of developing a familial lymphedema, by detecting the presence of a missense mutation in the VEGFR-3 allele described in SEQ. ID: 1, at the following positions: C3360T, G2588A, G3141C, T3150C and G3164A, does not reasonably provide enablement for a method of screening for an increased risk of developing any and all familial lymphedemas by detecting the "presence or absence" of any mutation altering the sequence or expression of any VEGFR-3 allele. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argue (See page 9, paragraph 3) that the present invention teaches the C3360T, G2588A, G3141C, T3150C and G3164A mutations which are indicative of hereditary lymphedema in family members, having a specified lymphedema phenotype.

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Examiner agrees that for prediction in a specified family the invention is enabled but not for prediction of any and all familial lymphedemas.

Applicants argue that they did not claim that the absence of the mutation will confer susceptibility to lymphedema. (See page 11, paragraph 1). Examiner argues that the language of the claim recites the following, "presence, **or absence of a mutation altering the encoded amino acid sequence**", which embodies the fact that the absence of a mutation may confer an altered VEGFR-3, which may in turn confer susceptibility to lymphedema.

Applicants argue that they are enabled for oligonucleotides as small as 6 nucleotides to be probes for determining the propensity of developing familial lymphedema. (See page 12, paragraph 1). Applicants also argue that other examiners have determined that oligos as small as 6 nucleotides are suitable for such technologies. However, examiner maintains the rejection as it is not clear that any 6 nucleotide sequence will appropriately and accurately be predictive of any disease.

Therefore, claims 1-11, 14, 15, 18, 20, 21 remain rejected.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-11 and 14-17 remain rejected under 35 U.S.C. 112, second paragraph, as stated in Office action dated 2/14/01, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Applicants argue examiners rejection due to the recitation of the term "correlates". Examiner maintains the rejection because the term does not adequately define the invention. The term "correlates" does not bear the specificity as claimed in the instant invention.

Claims 14-17 stand rejected as it recites "a wild type" which indicates that there are several wild type VEGFR-3 sequences.

Conclusion

8. Claims 1-11, 14-18, 20, 21 remain rejected.
9. Claim 19 is allowed.
10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

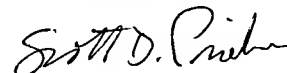
11. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (<http://www.uspto.gov>) and A CLEAN COPY OF ALL PENDING CLAIMS IS REQUESTED to facilitate further examination.

SCOTT D. PRIEBE, PH.D.



SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER